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by Larry F. Ellison

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Differences in cancer survival in Canada by sex

by Larry F. Ellison

Abstract

Background: Research in the United States and Europe has found that women have an advantage over men in surviving a diagnosis of cancer, but the issue has not been systematically studied in Canada.

Data and methods: Data are from the Canadian Cancer Registry, with mortality follow-up through record linkage to the Canadian Vital Statistics Death Database. The percentage unit difference in five-year relative survival ratios (RSRs) between women and men and the relative excess risk (RER) of death for women compared with men were used as measures of differences in cancer survival.

Results: A significant advantage for women compared with men was observed in 13 of the 18 cancers studied. Point estimates of RER were almost uniformly lower among those diagnosed at younger ages (15 to 54). For all cancers combined, women had a 13% lower excess risk of death—23% lower among women younger than 55. The overall advantage was greatest for thyroid cancer (RER = 0.31), skin melanoma (0.52) and Hodgkin lymphoma (0.65). The advantage for thyroid cancer was somewhat attenuated, though still significant, in earlier time periods. Bladder cancer was the only cancer for which women had a significant disadvantage (RER = 1.23); this excess risk seemed to be restricted to the first 12 to 18 months after diagnosis.

Interpretation: The reasons behind sex-specific differences in cancer survival are not well understood. Many explanations are possible, and differences are best explored on a cancer-by-cancer basis. The pronounced advantage for women at younger ages lends indirect support to a hypothesized hormonal influence.

Key words: Excess risk, gender differences, neoplasms, population-based, registries, relative survival, sex hormones, survival analysis

Studies in Europe,[1-3] the United States,[4] and Korea[5] have recently reported that women have an advantage over men in surviving a diagnosis of cancer. A biological advantage mediated through sex hormones has been proposed.[1,6-8] Another possibility is that the difference may, in part, reflect women's generally healthier attitudes and behaviours.[4,9-11] Whether the explanation is biological or cultural, or a combination of the two, has yet to be determined. Analyses of data from population-based cancer registries may be used to reduce, or at least better understand, sex-specific disparities in cancer prognosis.[1]

A potential advantage in cancer survival among women has not been systematically studied in Canada; overview articles have tended to focus on age-specific rather than sex-specific differences.[12,13] The sex-specific estimates that have been provided[14,15] were not age-standardized, thus making between-sex comparisons subject to confounding by age at diagnosis.

Based on data from the Canadian Cancer Registry, this report examines sex-specific differences in survival for all cancers combined and for 18 specific individual cancers or cancer groups. In addition to age-specific analyses, results are examined by time period of diagnosis. Although information on disease stage was not available, it was indirectly considered through an analysis by follow-up interval. The importance of adjusting for stage varies greatly by cancer.[4,5]

Methods

Data sources

Cancer incidence data are from the October 2011 version of the Canadian Cancer Registry, which includes primary cancer cases diagnosed from 1992 to 2009. The Canadian Cancer Registry is a dynamic, person-oriented, population-based database. Each provincial and territorial cancer registry supplies data on patients and tumours to Statistics Canada in a standard format and has the ability to add, update and delete records. To build and maintain the database, Statistics Canada applies a series of core edits and an internal record linkage process that identifies duplicates.

A file containing records of invasive cancer cases and *in situ* bladder cancer cases (the latter are included because of inconsistent tumour behaviour coding practices over time for this site and are reported for each province/territory except Ontario) was created using the multiple primary coding rules of the International Agency for Research on Cancer.[16] Cancer cases were defined based on the *International Classification of Diseases for Oncology, Third Edition*[17] and classified using Surveillance, Epidemiology, and End Results (SEER) Program grouping definitions.[18] Mortality follow-up through December 31, 2008 was carried out by record linkage to the Canadian Vital Statistics Death database (excluding deaths registered in the province of Quebec) and from information reported by the provincial/territorial cancer registries. For deaths reported by a provincial/territorial registry but not confirmed by the national record linkage, the date of death was assumed to be that submitted by the reporting registry. Application of the multiple primaries rules and record linkage were completed by Statistics Canada before the data file was made available to analysts.

Mortality data are from the Canadian Vital Statistics Death database. Deaths due to cancer were classified using the World Health Organization's *International Statistical Classification of Diseases and Related Health Problems—10th Revision (ICD-10)*[19] for deaths from 2000 onward, and *9th Revision (ICD-9)*[20] for deaths in earlier years.

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Expected survival, used in the calculation of relative survival ratios (RSRs), was derived from sex-specific complete annual[21] provincial life tables. Detail is provided elsewhere.[22]

Analytical techniques

Analyses were based on all primary cancers.[23-25] Data from the province of Quebec were excluded because the method of determining the date of diagnosis differed from that of the other provinces, and because of issues in correctly ascertaining the vital status of cases. Records were also excluded if: age at diagnosis was younger than 15 or older than 99; diagnosis was established through autopsy only (0.2%) or death certificate only (1.4%); or the year of birth or death was unknown (both extremely rare). Since this study examines differences by sex, cancers unique to one sex (genital system cancers) were excluded, as was breast cancer, which is rare in males.

Five-year RSRs for the 2004-to-2008 period were calculated with the period method[26]; estimates for earlier years were determined with the cohort method. The period method is commonly used to predict survival estimates for a recent period. It has been demonstrated to perform reasonably well, though estimates may be conservative for cancers with ongoing improvements in prognosis.[27-29]

Relative survival analyses were based on a publicly available algorithm[30] incorporating the Ederer II method[31] with minor adaptations to increase precision. Three-month subintervals were used for the first year of follow-up, then 6-month subintervals for the remaining 4 years, for a total of 12 subintervals. Cases with the same date of diagnosis and death (not including those previously omitted because they were diagnosed through autopsy only or death certificate only) were assigned one day of survival, because the program automatically excludes cases with zero days' survival. Exclusion of these cases would have biased the RSRs upward.

Although the definition of relative survival stipulates that the population comparison group should be "free of the specific disease under study,"[32] the population life tables included people previously diagnosed with cancer. The bias introduced into estimates of five-year RSRs by using such life tables is negligible for most individual cancers, but not for all cancers combined.[22,33,34] To counteract this bias, expected survival data used to estimate relative survival for all cancers combined were adjusted for cancer mortality in the general population.[22,33,34] The proportion of deaths among Canadian residents recorded as due to cancer, excluding genital system (ICD-10: C51-C58 and C60-C63; ICD-9: 179-187) and breast (C50; 174-175) cancers, by sex, five-year age group and year of death, was used for this purpose.

The sex and age group distributions of cases diagnosed from 1999 to 2008 that were eligible for survival analysis are provided for each cancer studied and for all cancers combined. These years were chosen to describe the full cohort potentially used in the five-year analyses, because the period method of survival does not pertain to any specific study population (cohort).[35] Sex-specific distributions of cases by cancer type were also provided. For confidentiality, case counts were randomly rounded to a base of five. Some cancer types were grouped for presentation according to the categories in the Canadian Cancer Statistics annual publication,[15] except that cancers of the colon and rectum are separate here.

RSRs were calculated for all ages combined and for five age groups: 15 to 44, 45 to 54, 55 to 64, 65 to 74, and 75 to 99. Age-standardized estimates were calculated using the direct method by weighting age-specific estimates for a given cancer to the age distribution of people diagnosed with that cancer from 2004 to 2008. Case-mix-standardized estimates were derived for analyses of all cancers combined to mitigate the effect of sex-specific differences in the distribution of cases by cancer type. They were obtained by weighting cancer-specific estimates to the cancer case distribution of the 19 cancers or cancer groups included.

Standard errors of RSRs were estimated by dividing the standard error of the observed survival (determined by

What is already known on this subject?

- In Europe and the United States, women have recently been described as having an advantage over men in surviving a diagnosis of cancer.
- Women's survival advantage is more pronounced when cancer is diagnosed before age 55.
- Differences in cancer prognosis by sex have not been systematically studied in Canada.

What does this study add?

- The prognosis after a diagnosis of cancer among Canadian residents was significantly better for women than men for a majority of individual cancers, and for all cancers combined.
- For the cancers studied, women's advantage was almost uniformly greater among those diagnosed at younger ages (15 to 54).
- Women's advantage was greatest for thyroid cancer, skin melanoma and Hodgkin lymphoma.
- The relatively large advantage for women diagnosed with thyroid cancer was somewhat attenuated, though still significant, in earlier time periods when the rate of diagnosis of this cancer was lower.
- A significant disadvantage for women emerged only for bladder cancer; the excess risk for women seemed to be restricted to the first 12 to 18 months after diagnosis.

Greenwood's method[36]) by expected survival.[37] For age-standardized RSRs, they were estimated by taking the square root of the sum of the squared weighted age-specific RSR standard errors.

The percentage-unit differences in five-year RSRs between women and men were rounded to one decimal place. The statistical significance of between-sex differences was determined via the Z test.

Generalized linear models with a Poisson error structure based on collapsed data and using exact survival times were employed to estimate the relative excess risk (RER) of dying after a cancer diagnosis for women, compared with men.[38] In addition to the analyses for all ages combined, separate analyses were conducted for younger (15 to 54) and older (55 to 99) age groups. Similar to other studies,[1,7,8] age 55 was used as a surrogate indicator of menopause. Stratified analyses were also conducted for three follow-up intervals: the first year after diagnosis; the second and third years combined after diagnosis, conditional on surviving the first year; and the fourth and fifth years combined after diagnosis, conditional on surviving the first three years.

All analyses were conducted in SAS 9.2 (SAS Institute Inc., Cary NC).

Results

Distribution of cases

From 1999 through 2008, for all cancers combined, the percentage diagnosed among women was 43.7%; among those diagnosed at ages 15 to 44, 53.4% were women (Table 1). For most of the individual cancers studied, the percentage of women ranged from 25% to 50%; the exceptions were cancers of the thyroid (77.7%) and larynx (16.8%). The percentage of women was typically highest among the oldest (75 to 99) or youngest (15 to 44) age groups at diagnosis. For both sexes, the most commonly diagnosed cancers were lung and bronchus (lung) (19.8% of cases among men, 20.9% among women) and colon cancer (12.1% and 15.0%, respectively).

Non-model-based analysis

After adjustment for age, a significant survival advantage emerged for women in 13 of the 18 specific cancers studied for the 2004-to-2008 period; women had a significant disadvantage only for bladder cancer (Table 2). In terms of percentage unit difference, the greatest advantage for women was for skin melanoma (6.3), followed by cancers of the oral cavity and pharynx (oral cancer) (6.2), and non-Hodgkin lymphoma (5.8). Differences were not significant for multiple myeloma, leukemia, and cancers of the liver and larynx. For all cancers combined, the five-year age- and case-mix-standardized RSR among women (48.9%) significantly exceeded that among men (2.9 percentage units).

For all cancers combined, five-year RSRs were significantly higher among women than men in each age group (Table 3). Women's survival advantage was greatest for those diagnosed at ages 15 to 44 (10.9 percentage units) and decreased with advancing age to 1.6 per-

Table 1
Number of eligible cases,† distribution by sex and age group, and cancer-specific proportion by sex, Canada excluding Quebec, 1999-to-2008 period

	Age group (years)													
	15 to 99				15 to 44		45 to 54		55 to 64		65 to 74		75 to 99	
Cancer	Cases	% women	% of men‡	% of women‡	Cases	% women	Cases	% women	Cases	% women	Cases	% women	Cases	% women
All cancers§	**706,590**	**43.7**	**100.0**	**100.0**	**57,075**	**53.4**	**83,825**	**44.2**	**141,370**	**39.8**	**191,530**	**39.2**	**232,785**	**47.1**
Oral cavity and pharynx	24,665	32.4	4.2	2.6	2,415	39.0	4,710	26.3	6,160	26.9	5,780	30.4	5,600	42.8
Esophagus	10,795	26.7	2.0	0.9	300	16.6	1,170	17.8	2,370	18.7	3,185	24.3	3,775	37.5
Stomach	21,190	35.3	3.4	2.4	1,035	48.6	2,245	34.0	3,860	28.1	5,755	30.2	8,290	40.8
Colon	94,155	49.0	12.1	15.0	3,075	51.0	8,105	47.7	17,230	43.1	27,015	43.9	38,730	55.4
Rectum	44,720	38.4	6.9	5.6	1,845	45.5	5,600	39.5	10,170	33.1	12,865	33.2	14,245	45.5
Liver	8,750	24.5	1.7	0.7	410	24.7	1,490	15.3	2,050	19.4	2,520	24.6	2,285	34.7
Pancreas	24,000	50.4	3.0	3.9	680	46.2	2,210	42.3	4,535	41.4	6,730	46.1	9,845	59.6
Larynx	7,190	16.8	1.5	0.4	190	22.2	885	16.6	2,010	15.7	2,345	16.9	1,760	17.7
Lung and bronchus	143,465	45.0	19.8	20.9	2,725	56.1	12,615	51.8	31,130	45.6	48,535	42.6	48,460	44.7
Skin melanoma	36,310	47.0	4.8	5.5	7,445	59.5	7,085	51.2	7,190	41.4	6,960	38.2	7,630	44.1
Bladder (including *in situ*)	42,235	25.2	7.9	3.5	1,040	34.0	3,170	26.6	7,510	24.5	12,610	21.7	17,910	27.3
Kidney and renal pelvis	28,565	39.0	4.4	3.6	2,190	39.2	4,735	35.2	6,960	34.5	7,425	38.7	7,255	46.0
Brain and other nervous system	15,815	43.3	2.3	2.2	3,500	42.4	2,615	39.2	3,295	40.5	3,265	41.4	3,145	52.8
Thyroid	24,845	77.7	1.4	6.3	10,605	82.5	6,080	78.7	4,200	72.9	2,480	66.6	1,480	72.2
Hodgkin lymphoma	6,210	45.0	0.9	0.9	3,805	46.6	755	35.8	610	42.5	545	42.0	495	53.4
Non-Hodgkin lymphoma	45,400	45.7	6.2	6.7	5,195	41.2	6,420	41.7	9,300	44.1	11,160	44.5	13,330	51.5
Multiple myeloma	13,530	45.3	1.9	2.0	395	40.8	1,335	41.6	2,700	40.9	3,820	43.9	5,285	49.8
Leukemia	29,540	41.4	4.3	4.0	3,265	41.9	3,345	38.2	5,445	37.4	7,270	38.5	10,225	46.6
Other§ and unknown	85,210	46.8	11.4	12.9	6,965	47.2	9,255	45.6	14,660	43.3	21,280	42.5	33,050	51.3

†cases diagnosed during 1999-to-2008 period that were potentially eligible for period survival analysis from 2004 to 2008; case counts randomly rounded to base of 5 for confidentiality
‡ sex-specific distribution of cancer cases by cancer type
§ excluding genital system cancers and breast cancer
Source: Canadian Cancer Registry database.

Table 2
Predicted five-year relative survival ratios (RSRs) for women and percentage unit superiority of estimates to corresponding estimates for men, by cancer, ages 15 to 99, Canada excluding Quebec, 2004-to-2008 period[†]

	Crude RSR				Age-standardized RSR			
		Women - Men				Women - Men		
			95% confidence interval				95% confidence interval	
Cancer	Women (%)	% units	from	to	Women (%)	% units	from	to
All cancers[‡]	**49.6**	**4.6**	**4.2**	**4.9**	**48.4**	**3.8**	**3.5**	**4.2**
Case-mix-standardized	**48.8**	**2.3**	**1.9**	**2.6**	**48.9**	**2.9**	**2.6**	**3.3**
Oral cavity and pharynx	66.4	5.3	3.2	7.4	66.6	6.2	4.1	8.3
Esophagus	15.0	1.8	-0.6	4.2	16.8	3.9	1.3	6.5
Stomach	26.5	3.2	1.2	5.1	26.6	3.6	1.6	5.5
Colon	63.4	0.8	-0.3	1.9	63.9	1.7	0.5	2.8
Rectum	65.3	2.5	1.0	4.1	65.7	3.5	1.9	5.1
Liver	18.4	-0.8	-3.8	2.1	19.3	1.5	-1.5	4.5
Pancreas	7.4	0.8	-0.2	1.8	7.7	1.4	0.3	2.4
Larynx	62.4	-1.7	-6.6	3.2	62.2	-2.2	-7.1	2.8
Lung and bronchus	19.4	5.7	5.1	6.3	19.1	5.4	4.8	6.0
Skin melanoma	92.2	6.8	5.5	8.1	91.7	6.3	4.8	7.7
Bladder (including *in situ*)	67.8	-5.0	-6.8	-3.2	68.1	-4.3	-6.1	-2.5
Kidney and renal pelvis	68.0	1.4	-0.4	3.2	68.4	2.8	0.9	4.6
Brain and other nervous system	27.7	4.5	2.5	6.6	27.3	5.5	3.7	7.3
Thyroid	98.8	4.1	2.9	5.4	98.6	3.2	2.0	4.4
Hodgkin lymphoma	87.3	4.2	1.5	6.9	87.1	4.8	2.3	7.3
Non-Hodgkin lymphoma	66.2	3.8	2.4	5.3	66.6	5.8	4.3	7.3
Multiple myeloma	38.9	-1.7	-4.4	1.0	39.1	0.6	-2.0	3.3
Leukemia	56.9	-0.5	-2.4	1.4	56.7	1.1	-0.8	3.0
Other[‡] and unknown	38.9	0.0	-1.0	1.1	38.5	0.8	-0.2	1.8

[†] period method of survival analysis used
[‡] excluding genital system cancers and breast cancer
Sources: Canadian Cancer Registry database; life tables; Canadian Vital Statistics Death database.

centage units among those diagnosed at ages 75 to 99. Adjusting for case-mix notably attenuated the advantage at ages 15 to 44 (a 6.8-percentage-unit reduction to 4.1) and 45 to 54 (2.8-unit reduction to 5.6). Nonetheless, women's survival advantage remained statistically significant in each age group.

For skin melanoma, non-Hodgkin lymphoma and lung cancer, women had a significant survival advantage in each age group; for brain and other nervous system cancers, the advantage was present in all but the 75-to-99 age group (p-value = 0.10). For oral cancer—reported above as having the second greatest age-standardized survival advantage for women—no significant advantage was observed among those diagnosed at ages 65 to 74 (p-value = 0.08) or 75 to 99 (p-value = 0.10). A significant survival disadvantage for women was found for those diagnosed with bladder cancer at ages 15 to 44 or 75 to 99 (7.7 and 8.8 percentage units, respectively). For laryngeal cancer, a non-significant (p-value = 0.06) disadvantage of 11.5 percentage units for women was observed in the 75-to-99 age group.

Model-based analysis

The model-based analysis identified the same 13 cancers as having a statistically significant survival advantage among women (Table 4). For all cancers combined, women's RER of death compared with men was significantly lower (0.87). Women's RER was lowest for thyroid cancer (RER = 0.31), skin melanoma (0.52) and Hodgkin lymphoma (0.65), followed by oral cancer, lung cancer, non-Hodgkin lymphoma, and brain and other nervous system cancers, for which RERs ranged from 0.78 to 0.81. Again, a significant disadvantage was evident for bladder cancer (RER = 1.23). RERs were not statistically significant for multiple myeloma, leukemia and cancers of the liver, and larynx.

A greater advantage (RER = 0.77) was observed for women when the analysis was restricted to the 15-to-54 age group, although the advantage was also significant for those diagnosed at ages 55 to 99. For the cancers for which women had an overall advantage, significant advantages were observed among both broad age groups. For every cancer studied except leukemia, point estimates of RER were lower among those diagnosed at ages 15 to 54 than at ages 55 to 99. Women's disadvantage for bladder cancer was similar in the younger and older age groups, though statistically significant only in the latter. However, an analysis of all five age groups revealed statistically significant results for those diagnosed at ages 15 to 44 (RER = 1.80) or 75 to 99 (1.41); otherwise, disadvantages were not significant (data not shown).

Significant advantages for women in the RER of death were observed for each follow-up interval for all cancers combined. However, the advantage was smaller in the first year after diagnosis (Table 5). Hodgkin lymphoma and multiple myeloma were the only two cancers for which the RER was lowest in the first year. For leukemia, a significant disadvantage was apparent for women in the first year (RER = 1.10), but significant advantages of 0.88 and 0.69 were found for the 1-to-3- and 3-to-5-year periods, respectively. For bladder cancer, women's higher RER of death was concentrated early in the follow-up.

A closer examination of the RER of death for bladder cancer using 6-month follow-up intervals (Figure 1) revealed women's excess risk to be greatest in the first half-year (RER = 1.62). Thereafter, the effect diminished—sharply between the first and second intervals (6 to 12 months) to 1.25, and then steadily between the second and fifth intervals (2.0 to 2.5 years). The excess risk was statistically significant in the 6-to-12-month interval, and narrowly missed significance in the 12-to-18 month interval. The evidence suggests that the

Table 3
Age-specific predicted five-year relative survival ratios (RSRs) for women and percentage-unit superiority of estimates to corresponding estimates for men, by cancer, ages 15 to 99, Canada excluding Quebec, 2004-to-2008 period†

	Age group (years)																			
	15 to 44				45 to 54				55 to 64				65 to 74				75 to 99			
		Women - Men				Women - Men				Women - Men				Women - Men				Women - Men		
			95% confidence interval				95% confidence interval				95% confidence interval				95% confidence interval				95% confidence interval	
Cancer	Women (%)	% units	from	to	Women (%)	% units	from	to	Women (%)	% units	from	to	Women (%)	% units	from	to	Women (%)	% units	from	to
All cancers‡	**83.6**	**10.9**	**9.9**	**11.8**	**65.1**	**8.4**	**7.5**	**9.4**	**53.7**	**4.4**	**3.6**	**5.2**	**44.3**	**2.2**	**1.5**	**2.9**	**35.2**	**1.6**	**0.9**	**2.3**
Case-mix-standardized	**80.5**	**4.1**	**3.2**	**5.0**	**62.7**	**5.6**	**4.8**	**6.5**	**53.9**	**4.4**	**3.7**	**5.1**	**46.0**	**2.9**	**2.3**	**3.6**	**36.6**	**0.8**	**0.1**	**1.5**
Oral cavity and pharynx	86.7	8.4	4.1	12.8	76.0	8.2	4.1	12.3	68.7	7.3	3.3	11.4	58.9	4.0	-0.4	8.4	56.5	4.6	-0.8	10.1
Esophagus	24.5	6.1	-12.2	24.3	21.0	4.8	-3.8	13.5	23.4	9.4	3.3	15.5	19.5	5.8	0.7	10.8	8.3	-1.7	-5.1	1.7
Stomach	39.2	8.3	-0.1	16.7	31.7	5.5	-0.2	11.3	30.8	5.2	0.6	9.8	30.7	5.8	1.9	9.8	19.4	0.3	-2.8	3.5
Colon	66.2	-3.0	-7.8	1.7	67.0	4.8	1.8	7.8	68.5	2.8	0.7	5.0	66.5	0.6	-1.3	2.5	59.3	1.6	-0.5	3.7
Rectum	72.9	6.6	0.5	12.8	72.7	7.9	4.3	11.5	71.2	2.7	-0.2	5.6	65.8	1.6	-1.2	4.5	57.9	3.6	0.3	6.9
Liver	55.5	18.3	2.0	34.7	28.8	2.9	-6.3	12.0	23.2	2.0	-4.8	8.7	16.9	1.0	-4.5	6.3	8.5	-1.3	-6.0	3.5
Pancreas	37.5	16.8	6.7	26.9	13.9	3.2	-0.9	7.3	8.9	1.2	-1.2	3.7	6.5	0.9	-1.0	2.7	4.8	0.5	-1.0	2.0
Larynx	F	F	F	F	69.8	1.1	-10.9	13.0	70.0	6.0	-2.4	14.5	55.8	-5.0	-13.3	3.4	54.9	-11.5	-23.6	0.7
Lung and bronchus	33.0	8.1	3.1	13.0	25.5	9.1	7.1	11.2	22.9	6.6	5.3	7.9	19.9	5.4	4.4	6.5	13.7	3.6	2.6	4.6
Skin melanoma	95.3	5.6	3.8	7.4	94.0	6.3	4.2	8.3	93.0	6.2	3.8	8.5	89.7	4.8	1.6	8.0	87.0	8.2	3.4	13.0
Bladder (including *in situ*)	81.3	-7.7	-14.6	-0.8	83.1	-0.0	-4.4	4.3	79.6	-1.1	-4.3	2.2	73.9	-0.5	-3.7	2.6	55.8	-8.8	-12.1	-5.4
Kidney and renal pelvis	89.1	6.6	2.4	10.9	80.3	5.8	2.2	9.4	75.3	6.4	3.1	9.7	66.3	1.8	-1.9	5.5	51.2	-2.6	-7.2	2.0
Brain and other nervous system	64.5	8.0	3.3	12.7	36.3	9.3	3.9	14.6	18.1	4.9	1.0	8.9	12.8	3.6	0.2	7.0	7.5	2.4	-0.5	5.2
Thyroid	99.8	0.4	-0.4	1.2	99.9	3.7	1.8	5.6	98.5	3.2	0.5	6.0	97.7	10.9	5.5	16.2	87.7	6.7	-4.9	18.4
Hodgkin lymphoma	95.9	2.1	0.0	4.1	95.2	12.0	5.5	18.4	80.9	6.4	-3.7	16.4	67.8	12.8	-0.7	26.3	38.6	2.6	-12.8	18.0
Non-Hodgkin lymphoma	83.8	6.0	2.9	9.0	81.1	6.0	3.0	9.0	77.1	7.8	5.1	10.6	65.6	7.0	4.0	9.9	47.8	3.4	0.0	6.7
Multiple myeloma	64.6	-1.7	-15.4	12.0	66.7	8.4	0.9	16.0	50.8	-1.6	-7.4	4.3	37.2	-2.7	-7.7	2.3	25.9	2.4	-2.0	6.7
Leukemia	71.0	4.1	-0.5	8.7	70.9	-3.0	-7.5	1.5	67.4	-1.7	-5.6	2.2	59.8	3.5	-0.2	7.3	41.4	1.4	-2.3	5.1
Other‡ and unknown	72.4	4.3	1.2	7.4	56.4	3.7	0.8	6.6	47.3	3.9	1.5	6.3	36.8	0.5	-1.5	2.6	25.4	-1.7	-3.4	0.1

† period method of survival analysis used
‡ excluding genital system cancers and breast cancer
F too unreliable to be published
Sources: Canadian Cancer Registry database; life tables; Canadian Vital Statistics Death database.

effect likely extends beyond the first year of follow-up, but not up to 18 months.

The relatively large advantage for women diagnosed with thyroid cancer in the 2004-to-2008 period was somewhat attenuated, though still significant, in earlier years. Among those with thyroid cancer, the RER of death for women compared with men fell from 0.59 in 1992-to-1996 to 0.41 in 1998-to-2002, and to a predicted 0.31 in 2004-to-2008 (Table 6). The change over the entire period was the largest among the cancers analyzed. Little change was observed for skin melanoma and bladder cancer, or for all cancers combined.

Discussion

This examination of cancer survival in Canada reveals an advantage for women compared with men in five-year relative survival for 13 of the 18 cancers studied. The RER of death advantage was greatest for thyroid cancer and skin melanoma; women had a significant disadvantage only for bladder cancer. For all cancers combined, women had a 13% lower RER of death.

In an analysis of data from the EUROCARE-4 project, Micheli et al. also observed a general survival advantage for women, although the difference between the sexes was smaller (RER = 0.95).[1] Results from the SEER database in the United States also pointed to an advantage for women, though no overall estimate was provided.[4] In Korea, a 9% lower RER of death for women, which rose to 11% after adjustment for stage, was reported for all solid cancers.[5] In these studies, women's advantage was greatest for thyroid cancer or skin melanoma (restricting to commonly considered cancers); the greatest disadvantage was for bladder cancer.

Micheli et al. found a greater survival advantage among women diagnosed before age 55,[1] and speculated that biological factors were involved, specifically, female hormonal status. Sex

Table 4
Predicted five-year relative excess risks (RERs) of death for women compared with men, by cancer and age group, ages 15 to 99, Canada excluding Quebec, 2004-to-2008 period†

	Age group (years)								
	15 to 99			15 to 54			55 to 99		
		95% confidence interval			95% confidence interval			95% confidence interval	
Cancer	RER	from	to	RER	from	to	RER	from	to
All cancers‡	**0.87**	**0.86**	**0.87**	**0.77**	**0.75**	**0.80**	**0.87**	**0.87**	**0.88**
Oral cavity and pharynx	0.78	0.73	0.84	0.66	0.57	0.78	0.82	0.76	0.89
Esophagus	0.89	0.84	0.96	0.79	0.64	0.98	0.91	0.85	0.98
Stomach	0.90	0.86	0.95	0.86	0.77	0.98	0.91	0.86	0.96
Colon	0.94	0.80	0.97	0.89	0.82	0.98	0.94	0.91	0.98
Rectum	0.87	0.83	0.92	0.73	0.65	0.83	0.90	0.85	0.96
Liver	0.97	0.96	1.05	0.86	0.70	1.04	1.00	0.92	1.08
Pancreas	0.89	0.85	0.92	0.79	0.70	0.88	0.90	0.86	0.93
Larynx	1.02	0.87	1.20	0.79	0.50	1.27	1.06	0.89	1.26
Lung and bronchus	0.78	0.76	0.79	0.71	0.68	0.75	0.78	0.77	0.80
Skin melanoma	0.52	0.46	0.58	0.46	0.38	0.55	0.57	0.49	0.67
Bladder (including *in situ*)	1.23	1.15	1.31	1.18	0.93	1.50	1.23	1.15	1.32
Kidney and renal pelvis	0.87	0.81	0.92	0.68	0.58	0.81	0.91	0.85	0.97
Brain and other nervous system	0.81	0.77	0.86	0.77	0.70	0.85	0.83	0.78	0.88
Thyroid	0.31	0.23	0.44	0.12	0.04	0.33	0.38	0.27	0.53
Hodgkin lymphoma	0.65	0.53	0.79	0.52	0.36	0.76	0.71	0.56	0.90
Non-Hodgkin lymphoma	0.79	0.75	0.83	0.70	0.62	0.79	0.80	0.76	0.85
Multiple myeloma	0.95	0.89	1.02	0.81	0.64	1.02	0.97	0.90	1.04
Leukemia	0.98	0.93	1.04	1.02	0.89	1.16	0.98	0.92	1.04
Other‡ and unknown	0.98	0.95	1.00	0.86	0.80	0.92	1.00	0.97	1.02

† period method of survival analysis used
‡ excluding genital system cancers and breast cancer
Notes: All results were adjusted for age group. All cancers were also adjusted for case mix.
Sources: Canadian Cancer Registry database; life tables; Canadian Vital Statistics Death database.

Table 5
Predicted relative excess risks (RERs) of death for women compared with men, by cancer and follow-up interval, ages 15 to 99, Canada excluding Quebec, 2004-to-2008 period†

	Follow-up interval (years)								
	0 to 1			1 to 3			3 to 5		
		95% confidence interval			95% confidence interval			95% confidence interval	
Cancer	RER	from	to	RER	from	to	RER	from	to
All cancers‡	**0.92**	**0.91**	**0.93**	**0.86**	**0.84**	**0.88**	**0.85**	**0.81**	**0.89**
Oral cavity and pharynx	0.83	0.75	0.91	0.79	0.70	0.89	0.72	0.57	0.91
Esophagus	0.98	0.90	1.05	0.78	0.67	0.91	0.94	0.62	1.41
Stomach	1.01	0.96	1.07	0.80	0.72	0.88	0.77	0.59	1.00
Colon	1.01	0.97	1.05	0.95	0.89	1.01	0.81	0.72	0.91
Rectum	0.93	0.86	1.00	0.88	0.81	0.96	0.82	0.72	0.94
Liver	0.93	0.85	1.02	1.07	0.90	1.28	0.86	0.58	1.25
Pancreas	0.91	0.87	0.95	0.93	0.84	1.03	0.75	0.55	1.03
Larynx	1.01	0.79	1.28	0.92	0.71	1.21	1.22	0.83	1.80
Lung and bronchus	0.81	0.80	0.83	0.81	0.78	0.84	0.92	0.84	1.00
Skin melanoma	0.49	0.40	0.61	0.55	0.46	0.65	0.48	0.36	0.64
Bladder (including *in situ*)	1.47	1.36	1.60	1.04	0.92	1.18	0.94	0.74	1.21
Kidney and renal pelvis	0.93	0.86	1.00	0.77	0.67	0.88	0.92	0.73	1.15
Brain and other nervous system	0.95	0.90	1.01	0.72	0.65	0.80	0.80	0.63	1.01
Thyroid	0.43	0.32	0.57	0.23	0.09	0.60	..	..	..
Hodgkin lymphoma	0.56	0.43	0.73	0.87	0.60	1.27	0.74	0.43	1.27
Non-Hodgkin lymphoma	0.86	0.81	0.91	0.76	0.69	0.85	0.76	0.65	0.88
Multiple myeloma	0.92	0.84	1.01	1.00	0.89	1.12	1.03	0.87	1.22
Leukemia	1.10	1.04	1.17	0.88	0.77	1.00	0.69	0.56	0.87
Other‡ and unknown	1.01	0.98	1.04	0.97	0.91	1.03	0.94	0.84	1.06

† period method of survival analysis used
‡ excluding genital system cancers and breast cancer
.. data not available (model did not converge)
Notes: All results were adjusted for age group. All cancers were also adjusted for case mix.
Sources: Canadian Cancer Registry database; life tables; Canadian Vital Statistics Death database.

hormones have also been hypothesized to at least partially explain more favourable outcomes for women in other studies.[6-8] In the present study, point estimates of RER of death for women compared with men were almost uniformly lower among those diagnosed before age 55. These observations indirectly support the hypothesized hormonal influence.

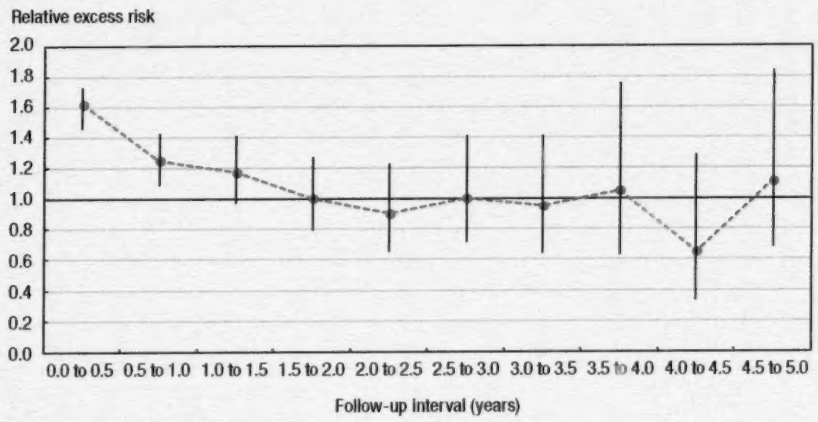
A number of alternative explanations for women's survival have been offered. For example, sex-specific differences in the prevalence of risk factors associated with both cancer and other co-morbid conditions (not accounted for in the relative survival analysis) can bias estimates of survival differences. An often cited example is tobacco use.[1,3,4] The distribution of lung cancer cases in this study was more similar between the sexes (45% women) than in the EUROCARE-4 data (30% women), suggesting less difference by sex in tobacco use in Canada. Thus, if a factor at all, tobacco use would likely have biased the current results to a lesser extent. In the case of bladder cancer, such a bias would have attenuated women's disadvantage.[39]

Another consideration is that incidence by subsite and/or histology for individual cancers can differ between the sexes. Confounding by case-mix may occur if survival also differs by these variables. The present study is also prone to this bias where individual cancers have been grouped (for example, oral cancer, leukemia). Although an adjustment for case-mix was made in the analyses for all cancers combined—with the greatest effect in the youngest age group—some residual confounding is possible.

It has also been theorized that women may be more likely to engage in health-promoting behaviours that could result in earlier and greater interaction with the health care system (for example, screening).[4,9-11] In some circumstances, this may mean an earlier stage of disease at diagnosis, and ultimately, a better prognosis.

A limitation of the present study is that stage at diagnosis could not be considered, as this information was not generally available in the Canadian Cancer Registry database for the period

Figure 1
Bladder cancer (including *in situ*) predicted relative excess risk of death for women compared with men, by follow-up interval, ages 15 to 99, Canada excluding Quebec, 2004-to-2008 period†



† period method of survival analysis used
I = 95% confidence interval
Sources: Canadian Cancer Registry database; life tables.

Table 6
Five-year relative excess risks (RERs) of death for women compared with men, by cancer and time period, ages 15 to 99, Canada excluding Quebec, 1992 to 2008†

	Time period								
	1992 to 1996			1998 to 2002			2004 to 2008		
		95% confidence interval			95% confidence interval			95% confidence interval	
Cancer	RER	from	to	RER	from	to	RER	from	to
All cancers‡	**0.87**	**0.87**	**0.88**	**0.87**	**0.86**	**0.87**	**0.87**	**0.86**	**0.87**
Oral cavity and pharynx	0.85	0.79	0.91	0.78	0.73	0.84	0.78	0.73	0.84
Esophagus	0.79	0.74	0.85	0.94	0.88	1.01	0.89	0.84	0.96
Stomach	0.85	0.81	0.89	0.89	0.85	0.93	0.90	0.86	0.95
Colon	0.96	0.92	0.99	0.96	0.92	0.99	0.94	0.80	0.97
Rectum	0.89	0.85	0.94	0.92	0.87	0.97	0.87	0.83	0.92
Liver	0.84	0.76	0.92	1.08	0.99	1.18	0.97	0.96	1.05
Pancreas	0.93	0.90	0.97	0.91	0.87	0.94	0.89	0.85	0.92
Larynx	1.12	0.96	1.30	1.03	0.89	1.20	1.02	0.87	1.20
Lung and bronchus	0.83	0.81	0.84	0.78	0.76	0.79	0.78	0.76	0.79
Skin melanoma	0.54	0.48	0.61	0.48	0.42	0.55	0.52	0.46	0.58
Bladder (including *in situ*)	1.23	1.14	1.33	1.11	1.04	1.19	1.23	1.15	1.31
Kidney and renal pelvis	0.88	0.82	0.95	0.86	0.80	0.92	0.87	0.81	0.92
Brain and other nervous system	0.78	0.74	0.83	0.81	0.77	0.85	0.81	0.77	0.86
Thyroid	0.59	0.46	0.76	0.41	0.32	0.54	0.31	0.23	0.44
Hodgkin lymphoma	0.74	0.60	0.90	0.85	0.69	1.04	0.65	0.53	0.79
Non-Hodgkin lymphoma	0.72	0.68	0.75	0.76	0.72	0.79	0.79	0.75	0.83
Multiple myeloma	0.85	0.79	0.91	0.90	0.84	0.96	0.95	0.89	1.02
Leukemia	1.00	0.95	1.06	0.89	0.84	0.94	0.98	0.93	1.04
Other‡ and unknown	0.94	0.92	0.97	1.00	0.98	1.03	0.98	0.95	1.00

† period method of survival analysis used for 2004-to-2008 period; otherwise cohort method used
‡ excluding genital system cancers and breast cancer
Notes: All results were adjusted for age group. All cancers were also adjusted for case mix.
Sources: Canadian Cancer Registry database; life tables; Canadian Vital Statistics Death database.

analyzed. In practice, the importance of adjusting for stage is highly dependent on the specific cancer type.[4,5] If stage was important, it seems reasonable that it would manifest itself most strongly earlier in the follow-up.[10] To some extent, the analysis by follow-up interval in the current study compensates for the absence of staging information.

The above noted factors are not a complete list of explanations for the results presented here and elsewhere. Potential explanations for sex-specific differences in survival are best considered on a cancer-by-cancer basis. While such a task is beyond the scope of this study, further consideration of the results for thyroid and bladder cancer is provided.

Among people diagnosed with thyroid cancer, a 69% lower RER of death was found for women. This cancer also had the largest change in RER from 1992 to 2008. Over this time span, the incidence of thyroid cancer in Canada rose at a faster rate than any other major cancer.[15,40] As in the EUROCARE-4 study, a greater reduction was observed among those diagnosed before age 55. Neither study adjusted for stage at diagnosis.

Jung et al.[5] observed a 47% lower RER of death for women diagnosed with thyroid cancer that remained virtually unchanged after adjustment for stage. Conversely, a similar age-adjusted RER for women relative to men for cancers of the endocrine system was almost halved when stage was included in the model.[4] Survival advantages for women that appeared in univariate analyses of papillary[8] and follicular cell[41] thyroid cancer did not persist when additional variables including stage were considered. However, Jonklaas et al.[8] observed better prognoses among women diagnosed with stage I or II disease before age 55 and hypothesized that age may influence the sex-survival relationship through hormonal changes associated with menopause. After finding that men were more likely to be diagnosed with more advanced disease and aggressive histological subtypes, Nilubol et al.[41]

postulated that thyroid tumour behaviour in men may be more aggressive. It is also possible that women seek medical attention earlier or undergo more thorough screening.[9]

Among the cancers examined in this study, bladder cancer was uniquely disadvantageous for women. Better prognoses among men have been found in most[1,4,5,42,43] but not all studies.[3] Noon et al.[44] found that women with high-risk disease fared worse in terms of cause-specific mortality than men. Significant disadvantages (8 to 9 percentage units) for women in five-year relative survival for bladder cancer were observed among those in the youngest and oldest age groups at diagnosis. These results are similar to those reported in the EUROCARE-4 study.[1] The data from Europe indicated significant but much smaller differences in the 45-to-54 and 65-to-74 age groups; such differences were not found in the present study. Higher risks among the youngest and oldest women relative to men were also observed in an analysis of Korean data.[5]

One theory for the poorer prognosis is that diagnosis of bladder cancer is more delayed, perhaps because of the rarity of this cancer in women relative to men.[4,44] Sex-specific disparities in referral patterns observed in two recent studies lend support to this theory.[45,46] Still, it is unlikely that women's less favourable prognosis can be entirely attributed to stage at diagnosis.[39] Where staging information has been available, adjustment for this variable resulted in attenuated yet still significant excess risk.[4,5,42] While stage was not accounted for in the present study, women's disadvantage appeared to be restricted to the first 12 to 18 months after diagnosis.

Conclusion

Survival was significantly better for women than men—particularly among those diagnosed at younger ages—for a majority of cancers in Canada. The reasons behind this disparity are not well understood. In general, the pronounced advantage for women at younger ages lends indirect support to a hypothesized hormonal influence. However, many explanations are possible, and differences are best explored on a cancer-by-cancer basis. ■

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